

# OBSERVATIONS ON URINARY AMOEBIASIS

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## INTRODUCTION

As a remote complication of amoebic dysentery there is no reason why the genito-urinary tract should not be affected, since it is recognised that the protozoal parasite from the large intestine may find its way through the portal system, to the liver most commonly of course, but also, as Rogers (1913) has pointed out, 'to the spleen or even more distant parts, such as the brain and other tissues, in any of which it may set up inflammatory processes ending in suppuration.' There is also a more direct route, to which Craig (1911) has called attention in his statement that there is 'no reason why any of the species [of *Entamoeba*] occurring in the intestine should not occasionally be found in the urine, reaching it through fistulae between the bladder and intestine, which may occur in cases of amoebic dysentery, or intestinal amoebae might reach the kidney or bladder through the surrounding tissues or through the blood stream.' Considering the wide distribution and frequency of occurrence of amoebic dysentery, it is a somewhat remarkable fact that very few cases have been recorded in which amoebae were found in the urine.

## PREVIOUS RECORDS

The earliest record of urinary amoebiasis appears to be that of Baelz (1883), who described an amoeba found in the blood-stained urine and in the vagina of a patient in Japan. This organism, called *Amoeba urogenitalis*, measured from  $23\mu$  to  $50\mu$  in diameter, was actively motile, and extruded pseudopodia that were short and blunt. Its cytoplasm was granular in appearance, it was phagocytic for red blood corpuscles, and it possessed a vesicular nucleus.

Similar cases appear to have been recorded by Jürgens, Kartulis, Posner, Wijnhoff, and Jeffries, but in the literature at our disposal here at Accra we are not able to consult the original papers. Craig (1911) in referring to the cases described by Baelz, Jürgens, Posner, and Kartulis, considers that it is still undecided whether the organism (*Entamoeba urogenitalis*) 'is entitled to specific rank, most authorities believing that the amoebae described by these authors were either *Entamoeba histolytica* or *Entamoeba tetragena*.' Fantham (1916), in a short memorandum in the 'British Medical Journal,' gives the following particulars of these cases:—'Jürgens found small mucous cysts, containing amoeboid bodies, in the bladder of an old woman suffering from chronic cystitis; they were also found in the vagina. Kartulis (1893) observed similar organisms in the sanguineous urine of a woman\* suffering from a tumour of the bladder; the organisms measured  $12\mu$  to  $20\mu$ , and exhibited slow pseudopodial movements, and a nucleus and vacuoles were seen after staining. Posner's case, a man, also passed blood stained urine, in which amoeboid granular bodies, about  $50\mu$  by  $28\mu$ , were present. The amoebae exhibited change of shape, and contained one or more nuclei as well as red blood corpuscles. The patient was under observation for over a year, during which the attacks recurred, and Posner concluded that the amoebae had penetrated into the pelvis of the kidney. Wijnhoff observed four cases of amoeburia in Utrecht, and Jeffries (1904) found similar cases in the United States.'

Craig (1911) mentions a case of infection of the bladder with *Entamoeba histolytica*, in which at the autopsy he found a minute fistula between the ulcerated intestine and the bladder.

Fischer (1914) found amoebae indistinguishable from *E. tetragena* in the urine of a Chinaman at Shanghai. The patient complained of painful micturition, and passed yellow and very acid urine containing a thick white sediment in which numerous amoebae were found. The parasites were from  $15\mu$  to  $25\mu$  in diameter; but no cysts were seen. There was no history of dysentery. Unfortunately the patient refused to remain under observation, so that a complete study of the case could not be made.

Lynn (1914) examined a somewhat similar case in a native man in Costa Rica. The patient complained of incontinence of urine and

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\* *Man* in the original.—EDD.

a burning sensation on micturating. There was a history of gonorrhoea two years previously, and a prostatic stricture was found. The urine contained blood, pus, and motile amoebae. No details were recorded of the morphology of the amoebae, but they were stated to have been *Entamoeba tetragena*. The infection was thought to have been conveyed by means of a syringe with which the patient washed out his own bladder having previously been used for rectal lavage. No amoebae were, however, found in the stool, although pus and blood were present, but as two doses of emetine had already been administered before this examination was made, it cannot be regarded as conclusive. There was no connexion between the intestinal tract and the bladder. The patient responded well to treatment (presumably emetine), and made a rapid recovery.

Finally, quite recently, Ward, Coles, and Friel (1916) have examined at Bournemouth and have recorded briefly a case of jaundice with albuminuria from Mudros, in which amoebae were found in the urine. The amoebae were 'light yellow-greenish bodies, circular or pear-shaped in outline, and of a markedly granular appearance.' There was no appreciable differentiation of endoplasm and ectoplasm, but some specimens that were watched carefully were seen to protrude a relatively clear pseudopodium that contrasted sharply with the semi-opaque granular endoplasm. The nucleus was easily seen, and was usually relatively large. The amoebae measured from  $8\mu$  or less to  $33\mu$  or more in diameter, but probably averaged about  $20\mu$  to  $25\mu$ . No cysts were seen in the urine. Cysts of *Entamoeba coli* were present in the faeces.

The authors consider this organism to be 'totally unlike *Entamoeba coli* or *Entamoeba histolytica*,' and proposed for it the new name *Amoeba urinae granulata*, but the details at present available are insufficient to distinguish the parasite from those previously described as occurring in the urine, and we agree with Fantham (1916) that the provisional name 'seems hardly necessary.'

The references enumerated above do not, of course, pretend to be a complete bibliography, but they are sufficient to show that amoebae have been detected in the urine in a number of cases, in white and yellow and dark skinned races, and in widely separated parts of the world, from China and Japan to Bournemouth and Utrecht.

## CASES RECENTLY EXAMINED ON THE GOLD COAST

During the last two years we have examined three cases of genito-urinary amoebiasis at Accra, Gold Coast Colony, West Africa.\* Two of the patients were negroes and one a European; all three were males.

The two cases in natives can be dismissed in a few words, as they attended hospital as out-patients only, and only a single specimen of urine from each was examined. In the first case the urine contained a considerable amount of white deposit, consisting chiefly of pus cells and some epithelial scales. No red blood corpuscles were noted, but a few highly refractile, greenish-yellow cells resembling amoebae were found. These cells were about  $20\mu$  in diameter and were mostly spherical, but a few were observed to extrude hyaline pseudopodia clearly differentiated from the granular cytoplasm of the rest of the organisms. Movements were decidedly sluggish, and no ingested corpuscles were seen. The nucleus was clearly visible in most of the specimens.

The second case was more interesting. The patient complained of the passage of blood-stained urine, and the examination was made with a view to determining if he was suffering from Bilharziasis. The urine contained a great many red blood corpuscles, pus cells, squamous epithelial cells and Bilharzia ova, and in addition a considerable number of amoebae. The amoebae were actively motile, and had ingested a large number of red corpuscles. They had the appearance of *E. histolytica*, and measured about  $20\mu$  to  $30\mu$  in diameter. No cysts were found. Unfortunately the patient had already left the hospital before the specimen of urine was examined, and as he did not return for further treatment it was impossible to obtain any history of the disease or any further material for study.

We have been more fortunate with our third case, the European, and have been able to keep him under observation for over two months; and as his condition presented some points of interest, we propose to record it rather more fully. We have to thank Dr. C. V. Le Fanu for bringing this case to our notice, and for sending the

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\* Since writing the above, two more cases have been examined in which amoebae were present in the urine. The parasite was in each case *E. histolytica* (*tetragena*). Both the patients were male natives, and one was suffering simultaneously from urinary schistosomiasis.

patient to us with the diagnosis 'amoebae in the urine' already made. We are also indebted to him for enabling us to study the condition in detail, for his careful examinations which assisted so greatly in its elucidation, and for his valuable advice and help at every stage of our investigation. The history of the case which follows is moreover based largely on his notes, and we have pleasure in expressing our gratitude to him for permission to make use of them.

The patient, a European official, 27 years of age, first came under observation on 16th May, 1916, complaining of frequency of micturition and the passage of white deposit with his urine. He was a man of very fair complexion and good physique. His heart, lungs, spleen, and liver were normal, and the function of the bowels was natural. There was no fistula. In his habits he was active, and during 1914 used to cycle twelve to fifteen miles a day over rough roads. He was in his third tour of service in the Gold Coast (a tour consisting of twelve months' residence in West Africa followed by five months' leave), and had enjoyed fairly good health except for a 'short fever, probably malaria,' while on leave in July, 1915, and an attack of malaria early in 1916. He had never suffered from dysentery, but mentioned that he had had 'a slight diarrhoea in November, 1914, lasting for eight days.'

He gave no history of gonorrhoea prior to the end of 1914, but in December of that year, three days after connexion, he felt acute pain between the root of the penis and the anus which lasted for three days. There was no discharge, but, nevertheless, he used an injection of permanganate for one month. The patient evidently believed that he had suffered from gonorrhoea, but as the diagnosis was not confirmed by bacteriological examination, and as he never had a typical discharge, it is possible that the condition may have been of a different nature. When last in England on leave, some months after the onset of his illness, he was examined bacteriologically for gonorrhoea, but with a negative result, and we have recently made the same examination on several occasions without detecting gonococci.

He remained free from symptoms until May, 1916, when, following a slight accident, he felt pain in the left groin. A few days later frequency of micturition set in, the desire to pass water

being constant for twenty-four hours, and three days later he passed a large quantity of 'mucus,' after which his condition improved.

The urine when first examined, that is on 16th May, 1916, was a yellow colour, showed an acid reaction, and contained some white sediment in which Gram-negative bacilli, a little mucus, crystals of calcium oxalate, a few leucocytes and some epithelial scales were observed. There were also some spherical cells in the deposit which were highly refractile and greenish in colour which were probably amoebae, but as no signs of motility were seen, we did not feel certain about this. About a month later, on 14th June, the patient returned with a recurrence of his symptoms. His urine was now faintly alkaline (probably as the result of treatment), yellow, and loaded with a white flocculent precipitate. In the deposit, which consisted mainly of pus cells and epithelial scales, there were a few red blood corpuscles and a large number of the spherical greenish bodies previously observed. These cells had a highly granular appearance, and varied greatly in size. Most of them appeared to be quiescent or dead, their nuclei being distinct, but when carefully watched a few were seen to extrude clear hyaline pseudopodia. A few contained ingested red blood corpuscles. A more complete account of these bodies, which were evidently amoebae, will be given later. No casts were found in the urine.

On the following day, 15th June, the desire to micturate frequently had ceased, and the urine was pale yellow coloured, faintly acid in reaction, and almost absolutely clear. One or two white flakes were found in it after centrifugalisation, and in these pus cells and a very few amoebae were present.

The desire to micturate frequently returned on the evening of the 15th June, and turbid urine was passed. On the following morning the irritability persisted, and amoebae were found in abundance in the urinary sediment. On this occasion the urine was passed into two glasses, and it was observed that whereas the first part contained a considerable amount of deposit, the last part was practically clear. This observation suggested that the pus and the amoebae did not come from the bladder itself nor from the kidneys, but from some area further forward.

For the next day or two the patient passed normal urine, but on 20th June there was a slight return of his symptoms. On examina-

tion no amoebae could be found in washings from the anterior urethra, but after vigorous rectal massage a quantity of white lumpy deposit was obtained, and in this large numbers of amoebae were found. The deposit also contained immobile spermatozoa.

This attack has been described in detail, as it was apparently typical of those to which the patient was subject.

With the three-glass test, Dr. Le Fanu observed that most of the deposit was passed into the second glass, the third being almost free from it. On rectal examination, both seminal vesicles were found to be enlarged. The testicles and epididymis were normal, and there was no glandular enlargement in the groins. These observations pointed to a lesion of the genito-urinary tract in the neighbourhood of the seminal vesicles.

The treatment adopted consisted of repeated rectal massage of the vesiculae and daily hypodermic injections of emetine (.5 grs.). During the months of June and July he had diurnal frequency of micturition on two or three occasions, but was not troubled at night. The urine passed was of an extremely pale colour and abnormally low specific gravity. When last seen, on 7th August, the patient expressed himself as feeling much better, and his general condition was quite satisfactory. The urine on this occasion was very light coloured, slightly turbid, and contained some short 'threads.' It was neutral in reaction, had a specific gravity of 1008, and showed a slight cloudiness on heating, due to the presence of phosphates, but no albumen was present. The deposit contained inflammatory cells and an occasional amoeboid body. Treatment then appeared to have benefited the patient, but up to the time of writing had not completely cured him of his amoebic infection.\*

#### THE MORPHOLOGY OF THE PARASITE FOUND IN THIS CASE

The morphology of the amoebae found in the urine of this patient was studied in freshly passed specimens and in fixed and stained preparations of the flaky deposit, and a brief account of the more important features observed is given below.

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\* The patient was completely cured by the third week in August.

*Size.* The amoebae varied greatly in size, but the majority were small. On one occasion, when the urine contained a large amount of white sediment in which innumerable amoebae were present, fifty individuals, taken as they came, were measured, and were found to average  $10\mu$  in diameter, ranging from  $7\mu$  to  $33\mu$ ; but more usually they averaged about  $20\mu$  in diameter, and some as large as  $40\mu$  were seen. Cysts were found, but none was seen containing more than four nuclei.

*Shape.* Most of the parasites, as seen in urine that had been passed some little time before examination, appeared to be in a quiescent condition, and were spherical. A few individuals were, however, pear-shaped, and others had thrust out pseudopodia which gave them an irregular outline. It was the presence of large spherical bodies of a slightly greenish colour that first drew our attention to the condition.

*The Protoplasm.* The appearance of the protoplasm varied, of course, with the age of the parasite, but there was always a distinct greenish-yellow tint and a conspicuously granular structure. In the spherical and quiescent individuals no distinction between ectoplasm and endoplasm could be made out, but in more irregularly-shaped parasites and in those exhibiting motility, it was clearly visible. The older amoebae were crowded with vacuoles, and the nucleus, which was usually easily seen, was often eccentric.

*The Cytoplasm.* The cytoplasm was composed of ectoplasm and endoplasm, but the distinction was not evident in the quiescent parasites. When the organism was moving, however, there was a distinct difference between the granular endoplasm and the hyaline glass-like ectoplasm of the pseudopodia; and in parasites of an oval or irregular shape even when not in motion, the same difference could be made out.

The endoplasm was granular, and contained a variety of ingested particles. A few of the parasites had ingested red blood corpuscles. Vacuoles were present in almost every amoeba, and were exceedingly numerous in the larger individuals. The vacuoles were not contractile.

*The Nucleus.* The nucleus was generally distinctly visible. It was large, and often situated somewhat eccentrically. Externally there was a well-defined nuclear membrane, refractile, and clearly



differentiated from the surrounding endoplasm. On the inner side of this membrane there was usually a large amount of chromatin arranged in irregular nodular masses, and throughout the nuclear substance similar chromatic matter was distributed. The karyosome was large, and showed a centriole.

*Vacuoles, &c.* Vacuoles were almost always present, and were generally very numerous. They were not contractile. The parasites were evidently actively phagocytic, and had ingested a variety of bodies, including erythrocytes.

*Motility.* The majority of the amoebae seen in the urine were quiescent, but a few when watched carefully were seen to extrude pseudopodia. The movements were sluggish, and did not result in active progression. The pseudopodia were blunt processes of ectoplasm with a clear glass-like appearance, and contained neither granules nor vacuoles.

*Stained preparations.* With haematoxylin or Romanovsky methods, or simply with methylene blue, the parasites stained well, but intensely. When taken directly from the urine, and stained in the ordinary way by the Romanovsky method (Giemsa), the whole organism was coloured a dark purplish hue, in which the nuclei could just be distinguished as almost black masses and the larger vacuoles as pink or purple discs; but after careful washing in salt solution the reaction became normal, the cytoplasm staining blue and the nuclei red. The action of the urine was evidently responsible for the peculiarities first observed, a conclusion that was confirmed by immersing in urine active amoebae (*E. histolytica*) from the faeces of a dysenteric patient, and finding that the same changes in staining reactions were produced.

In well stained specimens there was no characteristic difference between the reactions of the ectoplasm and endoplasm. The cytoplasm was highly vacuolated, and contained a number of food particles, &c., but although the urine was full of bacteria they did not appear to have been taken up by the amoebae to any considerable extent. Red blood corpuscles in various stages of digestion occurred in some of the parasites.

The structure of the nuclei varied a good deal, but in the majority of the amoebae it was of the *Entamoeba tetragena* type, and consisted of a centriole with a clear area round it, bounded by

the outer border of the karyosome, on which small particles of chromatin were collected. Outside this a reticulated zone reaching to the nuclear membrane, on which there was, as a rule, a considerable quantity of chromatin. Many of the variations observed were probably due to the changes occurring during the 'cycle of the karyosome' described by Hartmann, which we were able to follow in our preparations, but others may have been degenerative, and the result of the action of the urine on the organisms. The nuclear structure of *E. tetragena* has been so thoroughly studied, and is so well known, that it will be unnecessary to enter into greater detail here. Suffice it to say that most of the amoebae showed a nucleus of the *E. tetragena* type, and that such variations as were seen were an approximation, more or less complete, to the *E. histolytica* type.

As we have already explained, the kidneys and the bladder did not appear to be affected in this case, and we believe we were able to localise the lesion in the neighbourhood of the seminal vesicles. This fact must be taken into account in considering the characters of the amoebae, for when examined they were immersed in the urine, which was probably highly injurious to them. It is probable, indeed, that most of the parasites were already dead before they were examined, and that this explains the clear definition of the nucleus and the absence of motility in most of the cells. Those that were not actually killed were probably profoundly affected, and therefore exhibited only a slight degree of rather sluggish movement. It was actually demonstrated by taking active amoebae (*E. histolytica*) from the faeces of a dysenteric patient and immersing them in urine that changes were produced similar to those observed in this case.

Making all due allowance for the pernicious action of the urine, and considering the morphology of the parasites, their nuclear structure and the occurrence of cysts with four, but never more than four, nuclei, we believe that these amoebae cannot be differentiated from *Entamoeba histolytica* (*tetragena*).

### THE PROBABLE MODE OF INFECTION

The patient, as has been stated earlier, had never suffered from dysentery so far as he was aware, and at the time he came under our observation his faeces contained neither amoebae nor amoebic cysts; but about a month before his illness commenced he had a slight attack of diarrhoea, which lasted about eight days. This responded to simple treatment, and he thought nothing of it at the time. It is well known, however, that the remote complications of amoebic dysentery tend to occur 'months, or even years, after the primary dysenteric attack, which may have been a very slight one, so that the connexion with it is quite liable to be overlooked.'

Referring to amoebic hepatitis, Rogers (1913) points out that it 'not rarely occurs in subjects who give no history of ever having suffered from actual dysentery,' and if this is true of one of the remote complications of amoebic colitis, it is probably true of others. We are, therefore, inclined to believe that this patient may at some time have unconsciously harboured amoebae in his large intestine, and that they may have found their way thence, either directly or indirectly, to the neighbourhood of the seminal vesicles, setting up an inflammatory process ending in suppuration and the discharge of pus containing amoebae through the urethra.

### GENERAL CONSIDERATIONS

In the literature at our disposal, we have been able to find references, more or less complete, to about a dozen cases of urinary amoebiasis in addition to the three we have ourselves observed, and it may be of interest to consider them briefly.

In the majority of the patients the infection has been with *Entamoeba histolytica* (*tetragena*). This identification was definitely made by Craig, Fischer, and Lynn, and we have come to the same conclusion with regard to the parasite in our cases. The earlier records, those of Baelz, Jürgens, Posner, and Kartulis, are also generally believed to have referred to the same species. The morphology of the amoeba in the case recorded by Ward, Coles and

Friel has not yet been adequately described, and no identification can be made at present; but they have hitherto mentioned no characteristic that I have not observed in specimens of *E. histolytica* taken from the faeces after immersion in urine. It is possible that all the cases of urinary amoebiasis recorded may have been caused by *E. histolytica* (*tetragena*).

If the amoebae are not actually living in the urinary tract, but are in some neighbouring tissue from which they are discharged into the bladder and urethra, they may be greatly altered in appearance by contact with the urine, and may actually be dead before they are passed. This fact must not be forgotten in studying the morphology of the organisms, as they may be rendered unfamiliar-looking and difficult to identify.

Although the parasite may have been the same in all the cases, the site of the lesion has varied. In Posner's case there were casts in the urine, and the kidneys seemed undoubtedly to have been affected. In several other cases the lesion was equally certainly in the bladder. This was so in the original case, that of Baelz, in Jürgens' patient who had small mucous cysts containing amoebae in the bladder, and in Kartulis' subject who had a vesicular tumour. Craig's case stands on a different plane, since a sinus was discovered at the autopsy which connected the bladder with the ulcerated intestine. In one of our cases, the patient suffering simultaneously from Bilharziosis, the infection was probably in the bladder. Cystitis, or some condition interfering with the proper function of the bladder, seems to have been present in all these cases, and it may be that the altered composition of the urine accompanying these conditions enabled the amoebae to lodge in this organ. Fischer's case is somewhat obscure, but the urine was very acid, so that it seems probable that the parasites were not located in the bladder itself. Lynn's case, in which there was a burning sensation on micturating, and which was complicated by a prostatic stricture, may have been due to a lesion in the urethra. Our case, in a European, is the only one of the series in which the lesion was definitely localised in the neighbourhood of the urethra. We have stated our reasons for believing that the amoebae were lodged in the vicinity of the seminal vesicles, and if we are correct in our interpretation of the facts the condition was rather a remote

complication than a direct amoebic infection, and the presence of the organisms in the urine was in a sense accidental.

The genito-urinary tract is liable to amoebic infection by several routes. The parasites may gain access directly either from the outside by way of the urethra or from an ulcerated intestine through the intermediate tissues, and indirectly from the bowel through the blood stream. In Baelz's case, the vagina was infected as well as the bladder, and he believed that the parasites had been introduced with water used for washing the parts. The vagina was also infected in Jürgens' patient, and the amoebae may have spread thence to the bladder. Craig's case was an example of the direct spread through the tissues from an ulcerated intestine. Our European patient may have obtained his infection from the intestine either directly, or more probably indirectly, through the blood.

As regards sex and age incidence, no conclusions can be drawn from so small a number of cases, especially as several of them occurred in countries where the majority of the patients seen would be adult males. Direct infection by way of the urethra, however, might be expected to be more common in women, and this does appear to have been the case.

Urinary amoebiasis may be due to a primary infection or secondary to amoebic dysentery. It would certainly seem that cystitis, tumour of the bladder, and gonorrhoea are predisposing causes.

ACCRA,

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